

a.) Amendment to the Claims:

1. (Previously Presented) A method for regenerating nerve comprising administering to a patient in need thereof, a therapeutically effective amount of a pharmaceutical composition which comprises a substance that inhibits the activity of GSK-3, as an active ingredient.

2. (Previously Presented) The method according to claim 1 wherein the pharmaceutical composition is a therapeutic drug for a neurological disease.

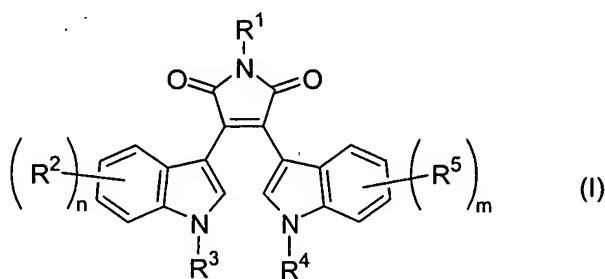
3. (Previously Presented) The method according to claim 2 wherein the neurological disease is selected from the group consisting of Parkinson's disease, Alzheimer's disease, Down's disease, cerebrovascular disorder, cerebral stroke, spinal cord injury, Huntington's chorea, multiple sclerosis, amyotrophic lateral sclerosis, epilepsy, anxiety disorder, schizophrenia, depression and manic depressive psychosis.

4. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is lithium or a pharmacologically acceptable salt thereof.

5. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 comprises a bisindolylmaleimide derivative, a 3-aryl-4-indolylmaleimide derivative, an indolocarbazole

derivative, an indolo[3,2-d][1]benzazepin-6(5H)-one derivative or an indirubin derivative, or a pharmacologically acceptable salt thereof.

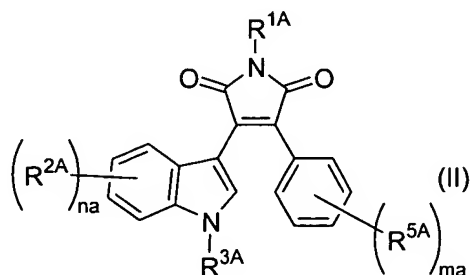
6. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 comprises a compound represented by the formula (I):



[wherein n and m may be the same or different, and represent an integer of 1 to 3; R¹, R³ and R⁴ may be the same or different, and represent hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, -COR⁶ (wherein R⁶ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl), -COOR⁷ (wherein R⁷ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl) or -OR⁸ (wherein R⁸ represents hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted aryl or substituted or unsubstituted cycloalkyl); R² and R⁵ may be the same or different, and represent hydrogen, substituted or unsubstituted lower alkyl, a substituted or unsubstituted lower alkenyl, substituted or unsubstituted lower alkoxy, substituted or unsubstituted lower alkoxycarbonyl, substituted or unsubstituted aryl, carboxy, halogen,

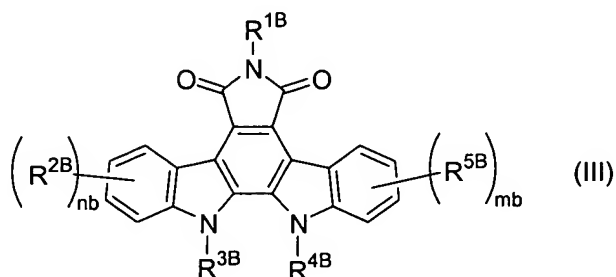
hydroxy, nitro, amino, or mono- or di-lower alkylamino; when n and m are 2 or 3, each of R^2 and R^5 may be the same or different],

a compound represented by the formula (II):

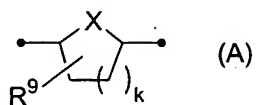


(wherein na, ma, R^{1A} , R^{2A} , R^{3A} and R^{5A} are as defined for the aforementioned n, m, R^1 , R^2 , R^3 and R^5 , respectively, or

a compound represented by the formula (III):



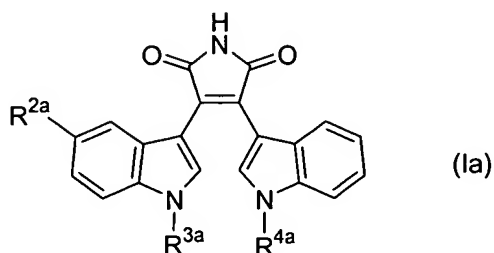
[wherein nb, mb, R^{1B} , R^{2B} and R^{5B} are as defined for the aforementioned n, m, R^1 , R^2 and R^5 , respectively; R^{3B} and R^{4B} may be the same or different, and represent hydrogen, substituted or unsubstituted lower alkyl, substituted or unsubstituted lower alkenyl, $-COR^6$, $-COOR^7$ or $-OR^8$, or R^{3B} and R^{4B} together form



(wherein k represents 1 or 2; X represents CH_2 , NH, an oxygen atom or a sulfur atom; R^9 represents hydroxy, carboxy, carbamoyl or lower alkoxy carbonyl)];

or a pharmacologically acceptable salt thereof.

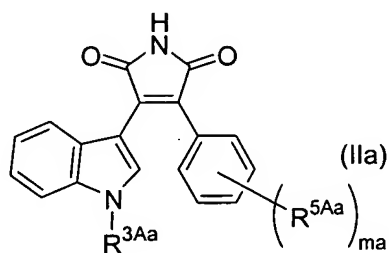
7. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is a compound represented by the formula (Ia):



(wherein R^{2a} represents hydrogen, lower alkoxy, lower alkoxycarbonyl, aryl or nitro; R^{3a} and R^{4a} may be the same or different, and represent substituted or unsubstituted lower alkyl),

or a pharmacologically acceptable salt thereof.

8. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is a compound represented by the formula (IIa):



(wherein R^{3Aa} represents substituted or unsubstituted lower alkyl; R^{5Aa} represents halogen),

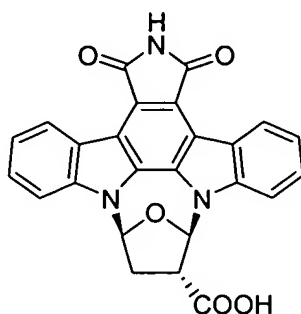
or a pharmacologically acceptable salt thereof.

(IIIa)

10. (Previously Presented) The method according to any one of claims

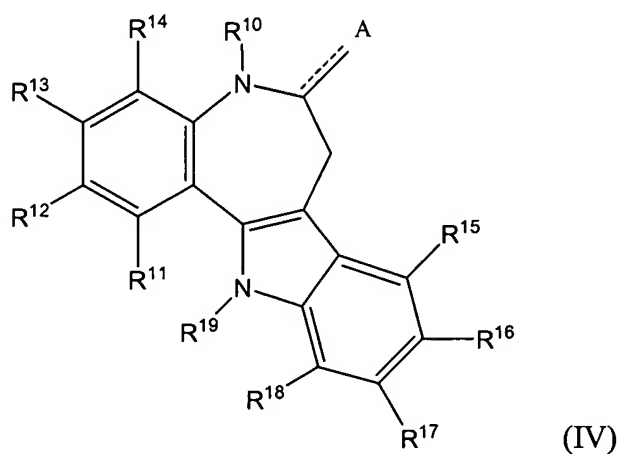
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pyrrole-2,5-dione, 3-(2-chlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2,4-dichlorophenyl)-4-(1-methylindole-3-yl)-1H-pyrrole-2,5-dione, 3-(2-chlorophenyl)-4-[1-(3-hydroxypropyl)indole-3-yl]-1H-pyrrole-2,5-dione, 4-[1-(3-aminopropyl)indole-3-yl]-3-(2-chlorophenyl)-1H-pyrrole-2,5-dione and



, or a pharmacologically acceptable salt thereof.

11. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 comprises a compound represented by the formula (IV):



[wherein A is oxygen or sulfur coupled to the right by a single or double bond; R¹⁰ is selected from the group consisting of hydrogen, aryl, lower aliphatic substituents, particularly alkyl and lower alkyl ester; R¹¹-R¹⁴ are independently selected

from the group consisting of alkoxy, amino, acyl, aliphatic substituents, particularly alkyl, alkenyl and alkynyl substituents, aliphatic alcohols, particularly alkyl alcohols, aliphatic nitriles, particularly alkyl nitriles, cyano, nitro, carboxyl, halogen, hydrogen, hydroxyl, imino and α,β -unsaturated ketones; R^{15} - R^{18} are independently selected from the group consisting of aliphatic substituents, particularly alkyl, alkenyl and alkynyl substituents, particularly lower aliphatic substituents, aliphatic alcohols, particularly alkyl alcohols, alkoxy, acyl, cyano, nitro, epoxy, haloalkyl groups, halogen, hydrogen and hydroxyl; R^{19} is selected from the group consisting of aliphatic groups, particularly lower alkyl groups, aliphatic alcohols, particularly alkyl alcohols, carboxylic acids and hydrogen],

or a pharmacologically acceptable salt thereof.

12. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is a compound selected from the group consisting of 7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 10-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 9-bromo-7,12-dihydro-4-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-4-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-4-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-

2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-
 indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-
 indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-
 indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2d][1]benzazepin-
 6(5H)-thione, 9-bromo-5,12-bis-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-d][1]-
 benzazepin-6(5H)-one, 9-bromo-12-(t-butyloxycarbonyl)-7,12-dihydro-indolo[3,2-
 d][1]benzazepin-6(5H)-one, 9-bromo-5,7-bis-(t-butyloxycarbonyl)-7,12-dihydro-indolo-
 [3,2-d][1]benzazepin-6(5H)-one, 9-bromo-5,7,12-tri-(t-butyloxycarbonyl)-7,12-dihydro-
 indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-5-
 methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-
 12-methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-
 dihydro-12-(2-hydroxyethyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-
 dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8,10-dichloro-7,12-dihydro-
 indolo[3,2d][1]benzazepin-6(5H)-one, 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-
 6(5H)-one, 9-bromo-7,12-dihydro-5-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 5-
 benzyl-9-bromo-7,12-dihydro-5-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-
 7,12-dihydro-12-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-12-ethyl-7,12-
 dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-(2-propenyl)-
 indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-methyl-indolo[3,2-d][1]-
 benzazepin-6(5H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-
 fluoro-7,12-dihydro-12-(2-propenyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-bromo-
 7,12-dihydro-indolo[3,2d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2-
 (methyliminoamine)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2-

(carboxylic acid)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-10-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-11-hydroxymethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-4-hydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,3-dimethoxy-9-nitro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,3-dimethoxy-9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-nitro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 3-(6-oxo-9-trifluoromethyl-5,6,7,12-tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)-propionitrile, 2-bromo-9-nitro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 3-(6-oxo-9-trifluoromethyl-5,6,7,12-tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)acrylonitrile, 2-(3-hydroxy-1-propenyl)-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-iodo-9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-(3-oxo-1-butenyl)-9-trifluoromethyl-7,12-tetrahydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-chloro-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 2-iodo-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-pyrido[3',2':4,5]pyrrolo[3,2-d][1]benzazepin-6(5H)-one, 11-methyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-[2-(1-hydroxycyclohexyl)ethinyl]-9-trifluoromethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-iodo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-ethyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-methyl-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one and 3-(6-oxo-9-trifluoromethyl-5,6,7,12-

tetrahydro-indolo[3,2-d][1]benzazepin-2-yl)acrylic acid, methyl ester, or a pharmacologically acceptable salt thereof.

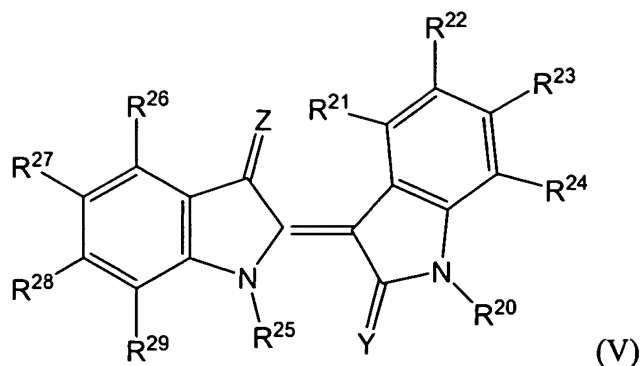
13. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is selected from the group consisting of 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indole-5(4H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 10-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 11-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-fluoro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-methyl-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-thione, 8,10-dichloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-(2-hydroxyethyl)-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dihydroxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-12-methyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-

7,12-dihydro-5-methyloxycarbonylmethyl-indolo[3,2-d][1]benzazepin-6(5H)-one and
7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one,
or a pharmacologically acceptable salt thereof.

14. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is selected from the group consisting of 9-cyano-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-bromo-7,12-dihydro-2,3-dimethoxy-indolo[3,2-d][1]benzazepin-6(5H)-one, 2-bromo-7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-2,3-dimethoxy-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 2,9-dibromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 7,12-dihydro-9-trifluoromethyl-indolo[3,2-d][1]benzazepin-6(5H)-one, 9-chloro-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, 8-bromo-6,11-dihydro-thieno[3',2':2,3]azepino[4,5-b]indol-5(4H)-one, 7,12-dihydro-9-methoxy-indolo[3,2-d][1]benzazepin-6(5H)-one,
or a pharmacologically acceptable salt thereof.

15. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is 9-bromo-7,12-dihydro-indolo[3,2-d][1]benzazepin-6(5H)-one, or a pharmacologically acceptable salt thereof.

16. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 comprises a compound represented by the formula (V):



[wherein R^{20} and R^{25} may be the same or different and represent hydrogen; halogen; a hydroxy group; a methylene hydroxy group; a straight or branched C_1 to C_{18} -alkyl or straight or branched C_1 to C_{18} -alkoxy or a methylenealkoxy group (wherein the alkoxy is straight or branched C_1 to C_{18}); a cycloalkyl group having 3 to 7 carbon which may have one or more heteroatoms a substituted or unsubstituted aryl, aralkyl or aryloxy group which may have one or more heteroatoms; a mono-, di- or trialkylsilyl group each independently having 1 to 6 carbon atoms within the straight or branched alkyl group; a mono-, di- or triarylsilyl group each independently having a substituted or unsubstituted aryl group; a trifluoromethyl group; -COM; -COOM; or a -CH₂COOM group (wherein M represents hydrogen, a straight or branched C_1 to C_{18} -alkyl group which may be substituted with one or more hydroxy and/or amino groups, or an aryl group, which may be substituted with one or more halogen, alkyl groups or alkoxy groups which may have one or more heteroatoms; an -NR³⁰R³¹ group (wherein R^{30} and R^{31} may be the same or different and represent a hydrogen atom, a C_1 to C_{18} straight or branched alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms); an acyl group; a -CH₂-NR³⁰R³¹ methyleneamino group; a benzyl group which may have one or more heteroatoms in the benzene ring; a methylenecycloalkyl group having 3 to 7 carbon atoms

which may have one or more heteroatoms; a physiological amino acid group coupled to a nitrogen atom as an amide; an O-glycoside or N-glycoside having glycoside of which being selected from monosaccharides or disaccharides; or a methylenesulfonate group; R^{21} , R^{22} , R^{23} , R^{24} , R^{26} , R^{27} , R^{28} and R^{29} may be the same or different and represent hydrogen; halogen; a hydroxy group; a nitroso group; a nitro group; an alkoxy group; a straight or branched C_1 to C_{18} alkyl group which may be substituted with one or more hydroxy and/or amino groups; a substituted or unsubstituted aryl group which may have one or more heteroatoms; a substituted or unsubstituted aralkyl group which may have one or more heteroatoms; a substituted or unsubstituted aryloxy group which may have one or more heteroatoms; a substituted or unsubstituted methylenearyloxy group which may have one or more heteroatoms; a cycloalkyl group having 3 to 7 carbon atoms which may have one or more heteroatoms; a methylenecycloalkyl group having 3 to 7 carbon atoms which may have one or more heteroatoms; a trifluoromethyl group; -COM; -COOM; or a CH_2COOM group (wherein M represents hydrogen, a straight or branched C_1 to C_{18} -alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, or an aryl group, which may be substituted with one or more halogen atoms, alkyl groups or alkoxy groups which may have one or more heteroatoms); an $-NR^{30}R^{31}$ group (wherein R^{30} and R^{31} which may be the same or different and represent hydrogen, a straight or branched C_1 to C_{18} -alkyl group which may be additionally substituted with one or more hydroxy and/or amino groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms, an acyl group, or form a part of cycloalkyl having 3 to 7 carbon atoms with the nitrogen atom which may have one or more heteroatoms); a $-CONR^{30}R^{31}$ group; a hydroxylamino group; a phosphate group; a phosphonate group; a sulfate group; a

sulfonate group; a sulfonamide group; an $\text{-SO}_2\text{NR}^{30}\text{R}^{31}$ group; an -N=N-R^{32} azo group (wherein R^{32} represents an aromatic group which may be substituted with one or more carboxyl, phosphoryl or sulfonate groups, or an O-glycoside or N-glycoside group having glycoside of which being selected from monosaccharides or disaccharides); or R^{20} and R^{24} , and R^{25} and R^{29} together form a ring which may have one to four CH_2 groups each independently substituted, respectively; Y and Z may be the same or different and represent an oxygen atom; a sulfur atom; a selenium atom; a tellurium atom; an NR^{33} group (wherein R^{33} represents hydrogen, a straight or branched C_1 to C_{18} alkyl group which may be substituted with one or more carboxyl, phosphoryl or sulfonate groups, a substituted or unsubstituted aryl group which may have one or more heteroatoms, an aralkyl group or a sulfonate group); or -NOR^{33}],

or a pharmacologically acceptable salt thereof.

17. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is a compound selected from the group consisting of indirubin, 5-iodo-indirubin, 5-bromo-indirubin, 5-chloro-indirubin, 5-fluoro-indirubin, 5-methyl-indirubin, 5-nitro-indirubin, 5- SO_3H -indirubin, 5'-bromo-indirubin, 5-5'-dibromo-indirubin and 5'-bromo-indirubin 5-sulfonic acid,

or a pharmacologically acceptable salt thereof.

18. (Currently Amended) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is a compound selected from

the group consisting of indirubin-3'-monooxime, 5-iodo-indirubin-3'-monooxime and 5-SO₃Na-indirubin-3'-monooxime,
or a pharmacologically acceptable salt thereof.

19. (Previously Presented) The method according to any one of claims 1 to 3 wherein the substance that inhibits the activity of GSK-3 is indirubin-3'-monooxime or a pharmacologically acceptable salt thereof.

Claims 20-37 (Cancelled)

38. (Previously Presented) A method of the manufacture of a neuron which comprises culturing a neural stem cell in the presence of the substance that inhibits the activity of GSK-3 to allow neogenesis of the neuron, and collecting the neuron from the culture.

Claims 39-41 (Cancelled)